REMARKS

I. Summary of the Office Action

Claims 1-42 were pending in the application.

Claims 1-42 were subject to restriction and/or election requirement. Applicants affirm without traverse the provisional election to prosecute the invention of Group I, claims 1-31.

Claims 32-42 were withdrawn from consideration.

Claims 1-31 were rejected.

The informal drawings filed on 01/26/2001 were objected to by the Draftsperson under 37 C.F.R. 1.84(l).

II. Status of Application

In response to the Office Action mailed July 8, 2003, claims 1-42 have been cancelled to expedite prosecution. New claims 43-48 have been added, and are discussed in greater detail below. New claim 43 generally corresponds to original claim 1. New claim 47 generally corresponds to original claim 11.

III. Aspects of the Claimed Invention

As defined by new claims 43 and 44, one aspect of applicants' invention provides an automated analytical system for sequential-injection sample analysis. The automated analytical system comprises (a) a multipositional stream-selection device; (b) a fluid-propulsion device, for conveying a fluid to and from the multipositional stream-selection device; (c) a source of sample; (d) a source of a reagent capable of reacting with a component of the sample to yield a reaction product detectable by the automated analytical system; (e) a detector, for generating from the reaction product a signal indicative of concentration of the component of the sample; and (f) a programmable electronic central processing unit for automatic control of fluid flow between the multipositional stream-selection device, the sample source, the regent source, and the detector.

The fluid-propulsion device, the sample source, the reagent source, and the detector are in fluid communication with the multipositional stream-selection device. The programmable electronic central processing unit is operationally connected to the multipositional stream-selection device. The programmable electronic sequence controller is operationally connected to the central processing unit. The programmable electronic central processing unit groups device events to form tasks, creates an electronic task manager as an electronic queue having a back and a front, adds new tasks to the back of the queue, retrieves a next task from the front of the queue, executes the task, and retrieves the next task for execution from the front of the queue.

As defined by new claims 45 and 46, a second aspect of the invention provides a programmable electronic controller for an automated analytical system. The controller comprises a programmable electronic central processing unit constructed and arranged to create an electronic task manager as an electronic queue having a back and a front, to group device events together to form tasks, to add new tasks to the back of the queue, to retrieve a next task for execution from the front of the queue, to execute the retrieved task, and to retrieve the next task from the front of the queue. A programmable electronic sequence controller is operationally connected to the central processing unit. The sequence controller is constructed and arranged to automatically determine sequence of events required in performing a plurality of tasks.

As defined by new claims 47 and 48, a third aspect of the invention provides an automated analytical system for sequential-injection sample analysis. The automated analytical system comprises (a) a multipositional stream-selection device; (b) a fluid-propulsion device, for conveying a fluid to and from the multipositional stream-selection device; (c) a source of sample; (d) a reservoir containing a lyophilized or concentrated reagent which, when dissolved in or diluted by a solvent, forms a reconstituted reagent that is capable of reacting with a component of the sample to form a reaction product detectable by the automated analytical system; (e) a source of solvent; (f) a detector, for generating from the reaction product a signal indicative of the concentration of the component of the sample; and (g) a central processing unit, for automatic control of fluid flow between the multipositional stream-selection device, the sample source, the

reservoir containing the lyophilized or concentrated reagent, the solvent source, and the detector.

The fluid-propulsion device, sample source, reagent reservoir, solvent source, and detector are in fluid communication with the multipositional stream-selection device. The central processing unit is operationally connected to the multipositional stream-selection device. The reagent reservoir includes a porous frit, to facilitate mixing of the solvent with the lyophilized or concentrated reagent, and to prevent residual solids from being drawn from the reagent reservoir with the reconstituted reagent.

IV. Analysis of the Prior Art

U.S. Patent No. 5,558,838 to Uffenheimer discloses a sample-preparation apparatus which includes a pair of valves. A first valve selectively communicates a sample tube with a vent/aspiration valve, or alternatively communicates a diluent pump with a reaction tube. By moving the first valve, one may selectively relieve a vacuum within a sample tube, aspirate a sample from the tube, or alternatively may drive a diluent and a sample into the reaction tube. The second valve is a vent/aspiration valve which selectively communicates the first valve to two distinct systems. A first system vents a vacuum in the sample tube, and a second system aspirates a sample from the sample tube. The second valve is actuated to initially relieve any vacuum in the sample tube, and is then actuated to connect the aspiration system to the sample tube to begin to withdraw a sample from the sample tube. At the same time, the diluent pump is filled. The shear valve is then moved to communicate the diluent pump to the reaction tube. The diluent pump is actuated to drive a diluent and a sample slug into the reaction tube, which preferably contains a predispensed reagent. A rinse system provides a rinse solution to the outer periphery of the needle, while the needle is connected to a source of suction, to withdraw the rinse fluid. A structure for holding and positioning the reaction tube provides a control signal indicating that a reaction tube is received in the reaction-tube structure. If no reaction tube is sensed, a controller deactivates the system such that no fluids are dispensed by the system.

U.S. Patent No. 5,104,808 to Laska et al. discloses a diagnostic instrument and method that indexes plural, sequentially-actuated reaction vessels stepwise to several

processing positions. The processing of the sample is controlled by a central processing unit according to different time-templates.

Tremmel et al. (U.S. Patent No. 5,171,538) disclose a reagent supply system for a medical instrument. The reagent supply system includes a reagent space provided on the instrument and reagent vessels, which are received in the reagent space. There is provided in the reagent space at least one reagent vessel compartment with a bottom, lateral guide elements, and a top guiding element, as well as a front stop. The instrument contains a fluid communication system for connection with a reagent vessel situated in the reagent vessel compartment. On the end face of the reagent vessel compartment is disposed a hollow needle near the bottom surface thereof, and extending in a direction parallel to the bottom surface. The reagent vessel has on its front wall, facing the end face, a pierceable seal with a pierceable elastic stopper.

Mack et al. (U.S. Patent No. 6,149,872) discloses a modular reagent cartridge which includes a plurality of reagent containers directly interconnected by integrally formed coupling devices. The connection is brought about by form-locking rail guides. At least one reagent vessel may exhibit a preferably snap-in connecting device, in order to produce a force-locking connection between a reagent cartridge and an analyzer. Such a reagent vessel, which can constitute to some extent a base element of the modular system, enables a force-locking connection between the reagent and the analyzer, which can be produced arbitrarily often and readily disconnected again owing to the special locking mechanism.

Dubus (U.S. Patent No. 6,054,326) discloses a fluid-testing analytical device and a method for using the device. The device includes, from its base up and in its upstanding configuration, a tube-holder for receiving at least one partially or totally transparent tube so that one wall or part thereof is visible; one or more tubes forming a closed testing and observation chamber, closure means for each tube, with a needle extending therethrough and a flange, surrounding the needle, of smaller diameter than the closure means; a substantially vertical raised portion forming peripheral and/or internal walls surrounding the needles and advantageously higher than the distance by which the needles project above the closure means; and, optionally, perforatable sheathes placed on the portion outside the closed chamber.

V. The Examiner's Rationale

In rejecting claims 1-7, 10, and 12 under 35 U.S.C. 102(b) over U.S. Patent No. 5,558,838 to Uffenheimer, the Examiner states that Uffenheimer discloses a sample preparation apparatus which includes a pair of valves. A first valve selectively communicates a sample tube with a vent/aspiration valve, or alternatively communicates a diluent pump with a reaction tube. By moving the first valve, one may selectively relieve a vacuum within a sample tube, aspirate a sample from the tube, or alternatively may drive a diluent and a sample into the reaction tube. The second valve is a vent/aspiration valve which selectively communicates the first valve to two distinct systems. A first system vents a vacuum in the sample tube, and a second system aspirates a sample from the sample tube. The second valve is actuated to initially relieve any vacuum in the sample tube, and is then actuated to connect the aspiration system to the sample tube to begin to withdraw a sample from the sample tube. At the same time, the diluent pump is filled. The shear valve is then moved to communicate the diluent pump to the reaction tube. The diluent pump is actuated to drive a diluent and a sample slug into the reaction tube, which preferably contains a predispensed reagent. This system simplifies the valving structure over the prior art systems. In addition, a unique rinse system provides a rinse solution to the outer periphery of the needle, while the needle is connected to a source of suction to withdraw the rinse fluid. Finally, a unique structure for holding and properly positioning the reaction tube provides a control signal indicating that a reaction tube is received in the reaction tube structure. If no reaction tube is sensed, a **controller** deactivates the system such that no fluids are dispensed by the system.

A sample preparation apparatus 20 is illustrated in Figure 1 including a control panel 22 for controlling the operation of the system. A tube guide 24 (cartridge support with alignment member) receives a closed sample tube 26 (reagent cartridge with a reservoir) including closure 28 (penetrable septa). Tube guide 24 guides sample tube 26 downwardly onto a **needle** 30 which punctures the closure 28. As will be explained below, any vacuum in the tube will be vented at that time. The sample may then be aspirated from the sample tube 26 and delivered to a reaction tube 32. A diluent pump 34 (fluid propulsion) communicates to the reaction tube 32 through a shear valve 36. Preferably, reaction tube 32 contains a predispensed reagent.

As shown in Figure 2A, **needle** 30 has punctured the closure 28 and line 41 communicates with the interior of sample tube 26 (reagent cartridge) through needle 30. As shown in Figures 2A and 2B, a rinse line 42 communicates with a chamber 44a: the outer periphery of the needle 30. Rinse line 42 is connected to a rinse fluid 46 through a pump 48. As will be explained below, after a sample is aspirated from sample tube 26, needle 30 is retracted and rinse fluid is delivered to chamber 44 to clean needle 30.

As also shown, a sample loop or passage 50 extends through shear valve 36. In addition, a groove 52 connects a diluent fluid 54 through a line 56 to a line 58 leading to diluent pump 34.

As shown in Figure 2A, shear valve 36 (a stream selection device) is in a position where passage 50 communicates line 41 (tubing) from needle 30 to a passage 60. Passage 60 will be termed a "valve passage" for purposes of this application as it connects the two main valves of this invention. Passage 60 passes through conductivity **detector** 61, and communicates with a vent/aspiration valve 62 having a passage 64. In the position shown in Figure 2A, passage 64 communicates passage 60 to a passage 66 leading to a check valve 68 which is in turn connected to atmosphere at 70. A conduit or line 72 is selectively communicated with passage 64 to communicate a pump 74 and waste reservoir 76 to line 60. In a second position of shear valve 36, a passage 59 is communicated through shear valve 36 to the diluent pump 34 to send a sample and diluent to the reaction tube 32.

In rejecting claims 4, 15, 16 and 27 as indefinite under 35 U.S.C. 112, the Examiner states that the terms "disposable" and "reusable" do not provide any further structure to the device. However, the Examiner suggests that applicants may intend to express that the cartridges are structurally capable of being readily removed or replaced, which implies that they have a detachable connection to the system.

In rejecting claim 11 under 35 U.S.C. 103(a) over U.S. Patent No. 5,558,838 to Uffenheimer in view of U.S. Patent No. 5,171,538 to Tremmel et al. or U.S. Patent No. 6,149,872 to Mack et al., the Examiner states that Uffenheimer does not disclose that the reagent cartridge contains a lyophilized reagent.

The Examiner states that Tremmel discloses a reagent supply system for a medical analytical instrument that includes a reagent space provided on the instrument and reagent vessels which are received in the reagent space. In the reagent space there is provided at least one reagent vessel compartment with a bottom, lateral guide elements, and a top guiding element, as well as a front stop. The instrument contains a fluid communication system for connection with a reagent vessel situated in the reagent vessel compartment. On the end face of the reagent vessel compartment is disposed a hollow needle near the bottom surface thereof and extending in a direction which is parallel to the bottom surface. The reagent vessel has on its front wall facing the end face a pierceable seal with a pierceable elastic stopper.

The Examiner states that Mack et al. disclose a modular reagent cartridge (10) which includes a plurality of reagent containers (12 to 18) directly interconnected by integrally formed coupling devices (22). The connection is brought about by form-locking rail guides. The invention relates to a reagent cartridge for the supply of ready-to-use, biochemical reagents in liquid form, whose purpose is to enable a simple loading into and use in a fully automatic analyzer.

The Examiner concludes that it would have been obvious to recognize that a cartridge may also be used to supply a reagent to the system of Uffenheimer.

In rejecting claim 20 under 35 U.S.C. 103(a) over U.S. Patent No. 5,558,838 to Uffenheimer in view of U.S. Patent No. 6,054,326 to Dubus and U.S. Patent No. 6,149,872 to Mack et al., the Examiner states that Uffenheimer does not disclose a reagent cartridge having a plurality of reagent reservoirs.

The Examiner states that Dubus discloses a fluid testing and analyzing device and a method therefor. The device includes, from its base up and in its upstanding configuration, a tube-holder (A) for receiving at least one partially or totally transparent tube (1) so that one wall or part thereof is visible; one or more tubes (1) forming a closed testing and observation chamber, closure means (4) for each tube, with a needle (3) extending therethrough and a flange (5), surrounding the needle, of smaller diameter than the closure means; a substantially vertical raised portion forming a peripheral and/or internal walls surrounding the needles (3) and advantageously higher than the

distance by which the needles project above the closure means (4); and, optionally, perforatable sheathes (11) placed on the portion outside the closed chamber (1). The device is particularly useful for human and animal biology applications.

Mack et al. disclose a modular reagent cartridge (10) which includes a plurality of reagent containers (12 to 18) directly interconnected by integrally formed coupling devices (22). The connection is brought about by form-locking rail guides. The invention relates to a reagent cartridge for the supply of ready-to-use, biochemical reagents in liquid form, whose purpose is to enable a simple loading into and use in a fully automatic analyzer.

The modular reagent cartridge 10, which is depicted in Figure 1, is constructed by connecting directly to each other several reagent vessels 12, 14, 16 and 18 by means of coupling devices, molded-on as one piece. In so doing, the reagent vessels 12, 14 and 16 are designed the same and comprise an essentially square-shaped vessel, which is sealed with a rubber disk 21, which is made of silicone, is slit, enables the filling of the reagent vessels in one special manufacturing step, and enables automatic removal of the aliquots in reagent positions in the analyzer. The type and shape of the slit, which can be designed in the shape of a cross, star or straight line, is preferably constructed in such a manner that it seals again following extraction of the filling mandrel of a filling machine or pipetting needle of the analyzer.

The Examiner concludes that it would have been obvious to modify the supply system of Uffenheimer to incorporate a multi-accessible cartridge support (as taught by Dubus) and a modular reagent cartridge as taught by Mack et al. in order to allow for different combinations of reagents to be supplied to the system.

VI. Support for New Claims

New claims 43-48 do not add new matter.

Antecedent basis for claim 43 is provided by the specification at least at page 5, lines 12-20; page 6, lines 24-30; page 11, lines 1-31; and by Figure 8.

Antecedent basis for new claim 44 is provided by the specification at least at page 7, lines 14-17; page 9, lines 4-16; and Figures 1 and 3.

Antecedent basis for new claim 45 is provided by the specification at least at page 11, lines 1-31, and by Figure 8.

Antecedent basis for new claim 46 is provided by the specification at least at page 7, lines 14-17; page 9, lines 4-16; and Figures 1 and 3.

Antecedent basis for claim 47 is provided by the specification at least at page 4, lines 18-20; page 5, lines 3-20; page 6, lines 24 –30; page 9, lines 17-23; and page 10, lines 11-27.

Antecedent basis for claim 48 (currently amended) is provided by the specification at least at page 10, lines 11-23.

VII. Discussions of New Claims

Because claims 2-10, 12-19, and 21-31 have been cancelled, applicants have not specifically replied to the Examiner's rejection of these claims in view of the cited references. The new claims, however, are discussed below with respect to the cited references.

A. Claim 43

New claim 43 generally corresponds to original independent claim 1. Claim 43, paragraph (f), recites a **programmable electronic** central processing unit, operationally connected to the multipositional stream-selection device and constructed and arranged for **automatic** control of fluid flow between the multipositional stream-selection device, the sample source, the reagent source, and the detector **by grouping device events together to form tasks**, creating an electronic **task manager** as an electronic queue having a back and a front, adding new **tasks** to the back of the queue, retrieving next **task** for execution from the front of the queue, executing the **task**, and retrieving the next **task** from the front of the queue.

It is submitted that none of the prior art, taken as single documents or as a combination of documents, anticipates, discloses, suggests, or makes obvious the central processing unit recited above.

Uffenheimer discloses a control panel (22) which is operated **manually, not automatically,** by a push-button (A,O,P) mechanism. **No overall automatic control is provided by this central processing unit.** (Figure 1; col. 3, lines 16-18; col. 5, line 60 to col. 6, line 13.)

Laska et al. disclose (but do not show) a central processing unit for controlling an automatic analytical device. (Col. 5, lines 19-23; col. 8, line 53 to col. 14, line 23.) Significantly, however, the central processing unit does **not** do so by **grouping device events together to form tasks**, creating an electronic **task manager** as an electronic queue having a back and a front, adding new **tasks** to the back of the queue, retrieving next **task** for execution from the front of the queue, executing the **task**, and retrieving the next **task** from the front of the queue, as recited by claim 43. This novel, unobvious, and unique property (**task management**) of the applicants' central processing unit confers a tremendous advantage in terms of operational efficiency over the central processing units disclosed by Uffenheimer, Laska et al., and other prior-art central processing units.

The difference in operating efficiency will be appreciated by comparing Figures 6A-1 through 6A-4 and 6B-1 through 6B-4 of the Laska patent with Figure 8 of applicant's specification. The enormous reduction in complexity of operation and in real time will be readily apparent to those skilled in the art when the respective drawings are compared.

Consideration and allowance of claim 43 are respectfully requested.

B. Claim 44

Claim 44 recites a programmable electronic sequence controller, operationally connected to the central processing unit, for automatically determining sequence of **events** required in performing a plurality of **tasks**.

It is submitted that none of the prior art, taken singly or in combination, anticipates, discloses, suggests, or makes obvious the sequence controller recited above.

Laska et al. disclose a diagnostic instrument that indexes plural, sequentially-actuated reaction vessels stepwise to several processing positions. The processing of the sample is controlled by a central processing unit according to different time-templates. (Col. 5, lines 19-23; col. 8, line 53 to col. 14, line 23.) This arrangement is entirely different from applicants' sequence controller, which, as above recited, automatically determines the sequence of **events** required in performing a plurality of **tasks**. Here, as in claim 43, what is being controlled and determined is the sequence of **events** which comprise a particular generic **task**. By grouping events into **tasks**, the central processing unit of claim 43 provides the sequence controller of claim 44 with a specific **group of events** which have been **organized** to perform **a particular and specific task**. After the sequence controller has organized **this particular set of events** timewise, the central processing unit can with extreme efficiency proceed to execute the **task**. The central processing unit and the sequence controller thus work **synergistically in combination** to provide an extremely efficient, time-conserving arrangement for an automated analytical system. Neither the sequence controller disclosed by Laska et al. nor any other sequence controller disclosed by any prior art known to applicants performs this efficient, novel, and unique function.

Consideration and allowance of claim 44 are respectfully requested.

C. Claim 45

This claim reiterates the recitation in claim 43 (re-presented), paragraph (f), of a programmable electronic central processing unit for an automated analytical system.

It is submitted that said programmable central processing unit is patentable per se, and that the arguments advanced above in support of claim 43 apply with equal force and validity to the instant claim. The novel and unique feature of **grouping events into tasks** which can then be controlled, ordered, sequenced electronically, and executed provides a central processing unit which far surpasses in efficiency and economy of operation any central processing unit known in the prior art.

Consideration and allowance of claim 45 are respectfully requested.

D. Claim 46

This claim reiterates claim 44. Accordingly, the arguments submitted above in support of claim 44 apply with equal force and validity to this dependent claim. The combination of the central processing unit of claim 45 and the sequence controller of claim 46 provides a unique and outstandingly effective electronic arrangement for **grouping and sequencing device events as executable tasks** which is entirely unanticipated or suggested by the prior art. It will be apparent to those skilled in the art that this synchronous combination of electronic devices results in a synergistic advance over the prior art.

Consideration and allowance of claim 46 are respectfully requested.

E. Claim 47

New claim 47 generally corresponds to original claim 11. Claim 47 recites (d) a reservoir containing a **lyophilized** or a **concentrated reagent** which, when **dissolved in or diluted by a solvent**, forms a **reconstituted reagent** that is capable of reacting with a component of the sample to form a reaction product detectable by the automated analytical system; and (e) a source of solvent for **dissolving or diluting** the **lyophilized** or **concentrated reagent**.

It is submitted that none of the prior art, including the patents to Tremmel et al. and to Mack et al., whether taken singly or in combination, discloses or suggests the above-recited elements. Tremmel et al. disclose reagents that are stored in reagent vessels and used without in any way altering their form, composition, or concentration. (Col. 4, line 7 to col. 5, line 2.) No mention is made of a **lyophilized** or a **concentrated** reagent which, when **dissolved in or diluted by a solvent**, forms a **reconstituted** reagent that is used in the analytical determinations. Mack et al. disclose a modular reaent cartridge (10) which is constructed for filling of the reagent vessels in one step, and automatic removal of aliquots of the reagent therefrom, **with no intermediate dissolution or dilution of the reagent**, as required by claim 47. (Col. 3, lines 32-41.) Throughout the patent, there is no mention whatsoever of using a **lyophilized** or **concentrated** reagent, **diluting or dissolving the r agent**, and using the resulting **reconstituted reagent** for the actual analyses.

The advantages of using one or more disposable cartridges containing **lyophilized** or **concentrated r agents** that are automatically **r constituted** provides a system that is suitable for use in a wide variety of application areas including the laboratory, operating room, and point-of-care environments. Use of such reagent cartridges reduces the minimum required technical expertise of users by automating the preparation of reagents. (Specification, page 5, lines 3-8.)

Consideration and allowance of claim 47 are respectfully requested.

F. Claim 48

Claim 48 recites a porous frit for the reagent reservoir, to facilitate mixing of the solvent with the lyophilized or concentrated reagent, and to prevent residual solids from being drawn from the reagent reservoir with the reconstituted reagent.

A lyophilized reagent is, by definition, a reagent that has been freeze-dried. When redissolved, there is always a possibility of undissolved residual solids being entrained with the reconstituted reagent solution. A frit facilitates mixing of the solvent with both a lyophilized and with a concentrated reagent, and furthermore prevents any residual solids from being drawn out of the reagent reservoir with the reconstituted reagent. (Specification, page 10, lines 11-26.)

It is submitted that none of the prior art, including the patents to Dubus and to Mack et al., taken either singly or in combination, discloses or suggests the use of a porous frit to facilitate mixing and/or to prevent residual solids from being drawn from a reagent reservoir, cartridge, or container. Indeed, as stated above in support of claim 47, Mack et al. make no provision for mixing a lyophilized or concentrated reagent with a solvent prior to use. Dubus teaches the introduction of a reagent, liquid or solid, into a tube **in which a sample is subsequently introduced without any further modification of the reagent**. (Col. 4, lines 43-49.) Clearly, this presents and describes an entirely different situation than that specified by claim 48; vis-à-vis, preliminary dissolution or dilution of a lyophilized or concentrated reagent **prior to use** for reaction with a component of a sample to generate a reaction product identifiable by the analytical system. In neither case (Dubus or Mack et al.) would a porous frit be appropriate or useful in the described analytical system.

Consideration and allowance of claim 48 are respectfully requested.

VIII. Drawings

In response to the Draftsperson's objection to the drawings under 37 C.F.R. 1.84(l), a corrected set of formal drawings is submitted herewith.

IX. Conclusion

In view of the foregoing, the claims pending in the application comply with the requirements of 35 U.S.C. § 112 and patentably define over the applied art. A Notice of Allowance is, therefore, respectfully requested. If the Examiner has any questions or believes a telephone conference would expedite prosecution of this application, the Examiner is encouraged to call the undersigned at (206) 359-3259.

Respectfully submitted,

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